General

Guideline Title

2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult.

Bibliographic Source(s)

Anderson TJ, Gregoire J, Hegele RA, Couture P, Mancini GB, McPherson R, Francis GA, Poirier P, Lau DC, Grover S, Genest J Jr, Carpentier AC, Dufour R, Gupta M, Ward R, Leiter LA, Lonn E, Ng DS, Pearson GJ, Yates GM, Stone JA, Ur E. 2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Can J Cardiol. 2013 Feb;29(2):151-67. [118 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Genest J, McPherson R, Frohlich J, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult - 2009 recommendations. Can J Cardiol 2009;25:567-79.

Recommendations

Major Recommendations

The grading of evidence (High, Moderate, Low, and Very Low) and strength of recommendations (Strong or Weak) are defined at the end of the "Major Recommendations" field.

Whom to Screen for Lipids

Screening of plasma lipids is recommended in adult men ≥40 and women ≥50 years of age or postmenopausal. See Figure 1 in the original guideline document for additional information. The presence of modifiable cardiovascular disease (CVD) risk factors (smoking, diabetes, arterial hypertension, obesity) is taken into account in the decision to screen for lipids at any age.

Risk Assessment

1. The expert panel recommends that a cardiovascular risk assessment, using the "10-Year Risk" provided by the Framingham model be completed every 3-5 years for men age 40-75, and women age 50-75 years. This should be modified (percent risk doubled) when family history of premature CVD is positive (i.e., first-degree relative <55 years for men and <65 years of age for women). A risk assessment might also be completed whenever a patient's expected risk status changes. Younger individuals with at least 1 risk factor for premature

CVD might also benefit from a risk assessment to motivate them to improve their lifestyle (Strong Recommendation, Moderate-Quality Evidence).
2. The expert panel recommends calculating and discussing a patient's "Cardiovascular Age" to improve the likelihood that patients will reach lipid targets and that poorly controlled hypertension will be treated (Strong Recommendation, High-Quality Evidence).

Values and Preferences

The primary evaluation of risk is the modified 10-year Framingham Risk Score (FRS). Considering the overlap in risk factors for diabetes, a simultaneous evaluation of cardiometabolic risk for diabetes might be useful to motivate lifestyle changes. It is well known that a 10-year risk does not fully account for risk in younger individuals. In these individuals, the calculation of a Cardiovascular Age has been shown to motivate subjects to achieve risk factor targets.

Levels of Risk

Low Risk (LR)

See Figure 2 in the original guideline document.

1. The expert panel recommends pharmacotherapy in LR individuals with low-density-lipoprotein cholesterol (LDL-C) ≥5.0 mmol/L, or if there is evidence of genetic dyslipidemia (such as familial hypercholesterolemia) (Strong Recommendation, Moderate-Quality Evidence).
2. The expert panel recommends ≥50% reduction of LDL-C in LR individuals for whom treatment is initiated (Strong Recommendation, Moderate-Quality Evidence).

Values and Preferences

This recommendation is unchanged from previous guidelines. Considering relatively less trial evidence in this group of subjects, individual practice will vary and will be dependent on the wishes of the patient and evaluation of the treating clinician. Subjects with a risk in the higher end of this category can have the risks/benefits of statin therapy discussed and might be offered statin therapy based on patient wishes and/or the judicious use of secondary testing.

Intermediate Risk (IR)

See Figure 3 in the original guideline document.

1. The expert panel recommends that the IR category include individuals with adjusted FRS ≥10% and <20% (Strong Recommendation, Moderate-Quality Evidence).
2. The expert panel recommends treating IR individuals with LDL-C ≥3.5 mmol/L (Strong Recommendation, Moderate-Quality Evidence).
3. In IR individuals with LDL-C <3.5 mmol/L, apolipoprotein B (apo B) ≥1.2 g/L, or non-high-density-lipoprotein cholesterol (non-HDL-C) ≥4.3 mmol/L is suggested to identify patients who might benefit from pharmacotherapy (Strong Recommendation, Moderate-Quality Evidence).
4. The expert panel recommends a target LDL-C ≤2.0 mmol/L or ≥50% reduction of LDL-C for IR individuals in whom treatment is initiated (Strong Recommendation, Moderate-Quality Evidence). Alternative target variables are apo B ≤0.8 g/L or non-HDL-C ≤2.6 mmol/L (Strong Recommendation, Moderate-Quality Evidence).

Values and Preferences

Non-HDL-C has been added as a second alternate treatment target because apo B is not available in some jurisdictions. Non-HDL-C is available without any additional cost or testing and there are increasing data to demonstrate its potential value. Therefore, it was decided to increase its profile in the guidelines. It is particularly useful where apo B is not available and in patients whose triglyceride level is greater than 1.5 mmol/L.

High Risk (HR)

1. The expert panel recommends that high risk be defined in subjects who have clinical atherosclerosis, abdominal aortic aneurysm, or an adjusted FRS of ≥20% (Strong Recommendation, High-Quality Evidence). The expert panel has also included diabetes of >15 years duration and age older than 30 years, diabetes with age older than 40 years, or the presence of microvascular disease, high risk kidney disease, or high risk hypertension (Strong Recommendation, Moderate-Quality Evidence).
2. The expert panel recommends a target LDL-C ≤2.0 mmol/L or ≥50% reduction of LDL-C for IR individuals in whom treatment is initiated (Strong Recommendation, Moderate-Quality Evidence).
3. The expert panel recommends that apo B ≤0.80 g/L or non-HDL-C ≤2.6 mmol/L be considered as alternative treatment targets for optimal risk reduction (Strong Recommendation, High-Quality Evidence).

Values and Preferences

The expert panel's decision to add chronic kidney disease (CKD) to the high risk category was based on significant emerging epidemiology data and the recently published Study of Heart and Renal Protection (SHARP) data. The treatment of dyslipidemia in subjects on hemodialysis remains controversial and individual judgement is required.

Secondary Testing in Risk Stratification

1. The expert panel recommends that secondary testing be considered for further risk assessment in "IR" patients (10%-19% FRS after adjustment for family history) who are not candidates for lipid treatment based on conventional risk factors or for whom treatment decisions are uncertain (Strong Recommendation, Moderate-Quality Evidence).
2. The expert panel suggests that secondary testing be considered for a selected subset of "LR to IR" patients (5%-9% FRS after adjustment for family history) for whom further risk assessment is indicated (e.g., strong family history of premature coronary artery disease [CAD], abdominal obesity, South Asian ancestry, or impaired glucose tolerance) (Weak/Conditional Recommendation, Low-Quality Evidence).

Values and Preferences

It is important to note that use of these tests should be viewed as optional and only to be used where decision-making will be directly affected (i.e., not in those in the high risk or lower risk groups [<5%]). The choice of which test to use depends on the clinical situation (see Supplemental Tables S4 and S5 [see the "Availability of Companion Documents" field]) and local expertise. In appropriate situations, hemoglobin A1c, urine albumin-to-creatinine ratio (ACR), and high-sensitivity C-reactive protein (hsCRP) can be helpful, are safe and inexpensive, and should be considered. For noninvasive testing a clinical suspicion of peripheral vascular disease should prompt arterial brachial index (ABI) testing. Individuals who have been inactive and wish to exercise could have an exercise stress test. Finally, recent evidence would suggest that coronary artery calcium (CAC) testing with computed tomography is superior to carotid ultrasound. However, given its expense and radiation exposure until further data are available it cannot be widely advocated.

Health Behaviours

1. The expert panel suggests that all individuals be encouraged to adopt healthy eating habits to lower their CVD risk: (1) moderate energy (caloric) intake to achieve and maintain a healthy body weight; (2) emphasize a diet rich in vegetables, fruit, whole-grain cereals, and polyunsaturated and monounsaturated oils, including Ω-3 fatty acids particularly from fish; (3) avoid trans fats, limit saturated and total fats to <7% and <30% of daily total energy (caloric) intake, respectively; (4) increase daily fibre intake to >30 g; (5) limit cholesterol intake to 200 mg daily for individuals with dyslipidemia or at increased CVD risk (Conditional Recommendation, Moderate-Quality Evidence).
2. The expert panel recommends the Mediterranean, Portfolio, or Dietary Approach to Stop Hypertension (DASH) diets to improve lipid profiles or decrease CVD risk (Strong Recommendation, High-quality Evidence), and for cholesterol-lowering consider increasing phytosterols, soluble fiber, soy, and nut intake.
3. The expert panel recommends that adults should accumulate at least 150 minutes of moderate-to-vigorous intensity aerobic physical activity per week, in bouts of 10 minutes or more to reduce CVD risk (Strong Recommendation, High-Quality Evidence).
4. The expert panel recommends smoking cessation (Strong Recommendation, Moderate-Quality Evidence), and limiting alcohol intake to 30 g or less per day (1-2 drinks) (Conditional Recommendation, Moderate-Quality Evidence).

Statin Intolerance and Adverse Effects

1. Because overall risk/benefit favours therapy in patients meeting criteria for lipid lowering therapy and cardiovascular risk reduction, the expert panel recommends that: (1) despite concerns about a variety of other possible adverse effects, all purported statin-associated symptoms should be evaluated systematically, incorporating observation during cessation, reinitiation (same or different statin, same or lower potency, same or decreased frequency of dosing) to identify a tolerated, statin-based therapy for chronic use (Strong Recommendation, Very Low-Quality Evidence); and (2) statins not be withheld on the basis of a potential, small risk of new-onset diabetes mellitus emerging during long-term therapy (Strong Recommendation, Very Low-Quality Evidence).
2. The expert panel does not recommend vitamins, minerals, or supplements for symptoms of myalgia perceived to be statin-associated (Strong Recommendation, Very Low-Quality Evidence).

Definitions:

Quality of Evidence*

High Quality: Further research is very unlikely to change confidence in the estimate of effect.

Moderate Quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

Low Quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Very Low Quality: Any estimate of effect is very uncertain.

Strength of Recommendations*

Strong Recommendation: Based on the available evidence, if clinicians are very certain that benefits do, or do not, outweigh risks and burdens they will make a strong recommendation.

Weak Recommendation: Based on the available evidence, if clinicians believe that benefits and risks and burdens are finely balanced, or appreciable uncertainty exists about the magnitude of benefits and risks, they must offer a weak recommendation. In addition, clinicians are becoming increasingly aware of the importance of patient values and preferences in clinical decision making. When, across the range of patient values, fully informed patients are liable to make different choices, guideline panels should offer weak recommendations.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Approach on who and how to screen for dyslipidemia
- Risk stratification by Framingham Risk Score (FRS) and phenotype
- Risk stratification for intermediate risk subjects

Scope

Disease/Condition(s)

- Dyslipidemia
- Cardiovascular disease

Guideline Category

Diagnosis

Prevention

Screening

Treatment

Clinical Specialty

Cardiology

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To present an updated version of the guidelines, incorporating new recommendations based on recent findings and harmonizing Canadian Cardiovascular Society (CCS) guidelines with those from other societies
- To increase the appropriate use of evidence-based cardiovascular disease event risk assessment in the management of dyslipidemia as a fundamental means of reducing global risk in the Canadian population

Target Population

Adult patients in the Canadian population at risk of dyslipidemia and cardiovascular disease

Interventions and Practices Considered

1. Screening of plasma lipids based on patient age and identifiable cardiovascular risk factors
2. Cardiovascular risk assessment using the "10-Year Risk" provided by the Framingham model
3. Calculating and discussing the patient's "Cardiovascular Age"
4. Establishing risk levels (low, intermediate, high)
5. Frequency of lipid monitoring
6. Establishing targets for low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (apo B), or non-high-density-lipoprotein cholesterol (non-HDL-C) based on risk level
7. Statin therapy
8. Secondary testing in risk stratification (e.g., lipoprotein [a], high-sensitivity C-reactive protein [hsCRP], hemoglobin A1c, urine albumin-to-creatinine ratio [ACR], exercise stress test, carotid ultrasound, arterial brachial index [ABI] testing, coronary artery calcium [CAC] testing with computed tomography)
9. Health behavior modification (e.g., healthy eating habits; Mediterranean, Portfolio, or Dietary Approach to Stop Hypertension [DASH] diets; physical exercise; smoking cessation; limiting alcohol intake)
10. Systematic evaluation of statin-associated symptoms to identify a tolerated, statin-based therapy for chronic use
11. Not withholding statins on the basis of a potential, small risk of new-onset diabetes mellitus
12. Vitamins, minerals, or supplements for symptoms of myalgia perceived to be statin-associated (not recommended)

Major Outcomes Considered

- Risk of cardiovascular disease
- Adverse effects and intolerance associated with statin therapy
- Major cardiovascular adverse events, including mortality

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature searches were completed between January 2012 and March 2012. The databases searched were: MEDLINE, MEDLINE – In Process, Ovid SP, PubMed, EMBASE, and Ovid Online.

Panel members were split into six working groups and separate searches were completed for each working group on the following topics using appropriate search terms:

- Health Behaviours
- Primary Prevention
- Risk Engine
- Secondary Prevention
- Secondary Testing
- Statin Intolerance

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence*

High Quality: Further research is very unlikely to change confidence in the estimate of effect.

Moderate Quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

Low Quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Very Low Quality: Any estimate of effect is very uncertain.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

In addition, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used as is now the standard established by the Canadian Cardiovascular Society.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The 2009 Canadian Cardiovascular Society (CCS) Dyslipidemia guidelines have been updated in the current document to reflect new advances. In addition, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used as is now the standard established by the Canadian Cardiovascular Society.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations*

Strong Recommendation: Based on the available evidence, if clinicians are very certain that benefits do, or do not, outweigh risks and burdens they will make a strong recommendation.

Weak Recommendation: Based on the available evidence, if clinicians believe that benefits and risks and burdens are finely balanced, or appreciable uncertainty exists about the magnitude of benefits and risks, they must offer a weak recommendation. In addition, clinicians are becoming increasingly aware of the importance of patient values and preferences in clinical decision making. When, across the range of patient values, fully informed patients are liable to make different choices, guideline panels should offer weak recommendations.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Cost Analysis

The guideline developers reviewed a published cost analysis.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

The Guidelines set forth by the primary panel were reviewed by a secondary panel of practitioners representing affiliated societies with a substantial interest in dyslipidemia treatment and cardiovascular risk reduction. Harmonization with recommendations from their representative societies and the Canadian Cardiovascular Harmonization of National Guidelines Endeavour (C-CHANGE) was encouraged and supported.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of dyslipidemia for the prevention of cardiovascular disease in the adult patient

Potential Harms

Statin Intolerance and Adverse Effects

The main intolerance issues with statins pertain to adverse muscle effects, but there are many other purported effects that are either uncommon or difficult to relate conclusively to statin therapy. Baseline transaminases (alanine aminotransferase [ALT]), creatinine, and creatine kinase are useful to monitor potential side effects associated with therapy. There is however no indication for routine repeat measures of ALT and creatine kinase in patients using statin therapy unless symptoms develop. Statins are not contraindicated in patients with mild to moderate elevations in ALT because of hepatic steatosis, chronic hepatitis C, or primary biliary cirrhosis. The following updates a recent, comprehensive review of these issues.

See the "Adverse Effects" section of the original guideline document for information about drug interactions, neurologic effects, and diabetes.

Qualifying Statements

Qualifying Statements

This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Pocket Guide/Reference Cards

Quick Reference Guides/Physician Guides

Slide Presentation

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 (revised 2013 Feb)

Guideline Developer(s)

Canadian Cardiovascular Society - Professional Association

Source(s) of Funding

The review was conducted under the direction of the Canadian Cardiovascular Society (CCS) completely at arm's length from industry.

Guideline Committee

Guidelines Expert Panel

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

The disclosure information of the authors and reviewers is available from the Canadian Cardiovascular Society (CCS) on the following Web sites: www.ccs.ca and/or www.ccsguidelineprograms.ca.

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Guideline Availability

Electronic copies: Available from the Canadian Journal of Cardiology Web site.

Availability of Companion Documents

The following are available:

- Supplemental material, including tables and a summary of recommendations, is available from the Canadian Journal of Cardiology Web site.
- A variety of resources, including a mobile app, slide decks in English and French, pockets guides in English and French, a Framingham Risk Score chart, the CIRCL CardioRisk Calculator™, and accredited E-learning programs are available from the Canadian Cardiovascular Society Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 10, 2013. The information was verified by the guideline developer on

October 10, 2013.

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